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Reference: EPA Document Control Number: 8EHQ-92-1237 SUPP

Dear Sir/Madam:

In May, 1991 the International Diatomite Producers Association (IDPA) reported to the EPA pursuant to Section 8(e) of the Toxic Substances Control Act (15 U.S.C. 2607(e)) the preliminary findings of a cohort mortality study of certain workers in the diatomite industry conducted by the University of Washington's Department of Environmental Health and directed by Dr. Harvey Checkoway. Supplemental information was provided in October, 1992, again in October, 1993, and further in December 1994. In the October 1992 submittal, EPA was provided with the Final Study Report issued by the investigators. The October 1993 and December 1994 submittals related to asbestos exposure to the cohort beyond that stated in the final report. In the December, 1994 submittal, EPA was provided with the final report providing the reconstruction of the asbestos exposure to the workers, by Dr. Graham Gibbs of Safety Health Environment International Consultants Corporation of Alberta, Canada.

Using the new data on asbestos exposure, a re-analysis of the original study data was conducted by Dr. Checkoway at the University of Washington. A re-analysis report, *Re-analysis of Lung Cancer Among Diatomaceous Earth Industry Workers with Consideration of Potential Asbestos Exposure*, co-authored by Drs. Checkoway and Gibbs has now been issued. A copy of that report is enclosed with this letter on behalf of the IDPA and its member companies.

The re-analysis included Standard Mortality Ratios (SMRs) relative to mortality rates in the U.S. for; the entire cohort; subsets of workers who had either "probable" or "definite" asbestos exposure; workers who had neither "probable" nor "definite" exposure to asbestos; joint strata of workers defined by cumulative exposures to crystalline silica and asbestos; and with reference to crystalline silica exposure after sequentially eliminating workers with various categories of asbestos exposure. SMR trend analyses were also conducted.

The overall lung cancer SMR was 1.41 (95% CI, 1.05-1.85) compared to national rates. The overall SMR for lung cancer in the original study was 1.43 (95% CI, 1.09-1.84). Some adjustments to the original cohort were necessitated by the available data and to account for

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workers previously known to have been exposed to asbestos. The lung cancer SMR for the group with no asbestos exposure was 1.13 (95% CI, 0.73-1.69); for the group with any asbestos exposure it was 1.78 (95% CI, 1.18-2.57). The cross-classified SMR results were numerically unstable because of the small numbers of observed lung cancers.

None of the SMR trends reached the conventional level of statistical significance. The authors noted that a risk gradient continued to be observed with crystalline silica among workers who had no apparent asbestos exposure, however, it is weakened from that reported previously (Checkoway et al, 1993) and no longer statistically significant. While the authors state that asbestos exposure was not an important confounder, the findings indicate that asbestos exposure may have contributed to the lung cancer risk among some members of the cohort.

In summary, the additional information gained from an in-depth assessment of possible exposures to asbestos experienced by the cohort has lead to a re-analysis of the original study report. Some of the excess lung cancer risk reported previously (Checkoway et al, 1993) can be attributed to asbestos exposure and the remaining numbers are weaker and lacking in statistical significance. A 5-year follow-up and radiographic study, sponsored by NIOSH, is currently in progress that should help to shed more light on the subject.

Please do not hesitate to contact the undersigned if you have any questions about this letter or if we can be of further assistance.

Sincerely,

Mel J. Mirliss
Executive Director

RE-ANALYSIS OF LUNG CANCER AMONG DIATOMACEOUS EARTH INDUSTRY WORKERS WITH CONSIDERATION OF POTENTIAL ASBESTOS EXPOSURE

FINAL REPORT

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February, 1996

Introduction

Following publication of the findings from the University of Washington cohort mortality study of diatomaceous earth (DE) workers [Checkoway et al., 1993], there were suggestions that exposures to asbestos at the Manville plant may not have been fully recognized, and thus not taken into account in the analysis. Mortality data for a group of 104 workers with known prior asbestos exposures, primarily from mixing operations at the Manville DE plant, were analyzed separately from the main cohort data, although the full extent of possible asbestos exposure was not known at the time of the study. Accordingly, the International Diatomite Producers Association (IDPA) commissioned Gibbs and Christensen to perform an in-depth assessment of possible exposures to asbestos experienced by the cohort. Details are provided in a report to the IDPA [Gibbs and Christensen, 1994].

The goal of our re-analysis was to examine the exposure-response relation between crystalline silica and lung cancer mortality, while taking into account potential confounding from asbestos exposure. Also of interest were the possibilities that asbestos may have an independent association with lung cancer among DE workers and that asbestos may act synergistically with crystalline silica on lung cancer risk.

Methods

The re-analysis was performed among 2266 white male workers from the former Manville (now Celite) plant in Lompoc, California. Those were workers for whom it was possible to estimate potential asbestos exposures in DE operations. In addition to females and non-whites, excluded from this group were 66 workers hired before 1930, 327 workers who had been employed at the Grefco plant (299 only at Grefco; 28 also at Manville), and 8 workers with known asbestos exposure from employment prior to working at the Manville DE plant. Information on asbestos exposure of Grefco workers was not available; thus, they were excluded. Workers employed before 1930 were excluded because Gibbs and Christensen [1994] reported that there had been some use of asbestos at the Manville plant during that period, but felt that the information available to them was inadequate to make job-specific exposure estimates. Included in the re-analysis were 89 Manville workers who had worked in the Mortar Plant or Experimental/Specialty Products areas where asbestos exposure was known to have occurred (in the original report, data for these workers had been analyzed separately from the main study cohort).

Jobs were classified according to asbestos exposure potential by the method of Gibbs and Christensen [1994]. This scheme provided a classification of jobs as "not" exposed, "probably" exposed, or "definitely" exposed. Jobs classified as "possibly" exposed were considered to be only remotely likely to involve asbestos exposure for individuals who held them [Gibbs and Christensen, 1994]. Such jobs were therefore treated as "not" exposed in the analysis. The exposure reconstruction method of Gibbs and Christensen also enabled semi-quantitative estimates of asbestos levels (fibers/ml) for each job. The term 'asbestos' has been used throughout this report to refer to chrysotile used in the production and to other fiber types occasionally encountered in the mill or as part of maintenance and other activities. No attempt has been made in the this re-analysis to examine the specific role of individual fiber types.

In the original study, some jobs had been combined because of similarity of tasks and silica exposures. Other than identification of the two work areas involving asbestos exposure (Mortar Plant, Experimental Plant/Specialty Products), the potential for asbestos exposure was not considered when work history data were assembled in the original study. There were approximately 15% of the jobs analyzed in the original report [Checkoway et al., 1993] that, according to Gibbs and Christensen [1994], included component jobs with varying asbestos exposure levels. These jobs were assigned asbestos exposure ratings (none, probable, definite) and intensity levels (fibers/ml) by determining a weighted average asbestos level for the component jobs. To illustrate, consider the hypothetical case where a job category used in the original analysis encompassed 2 component jobs with similar silica exposures, but varying estimated asbestos levels. The estimated asbestos exposure intensity values for the component jobs are 1.0 and 0.5 fiber/ml, and the corresponding percentage contributions of work time to the overall job category are, respectively, 75% and 25%. Then, the estimated level would be (1.0 x 75%) + (0.5 x 25%) = 0.875 fibers/ml. For the exposure ratings (not exposed, probable, definite), we assigned to the combined job category, and hence to each component job, the rating contributed by the majority of work time contributed by the component jobs. If in the preceding example, the first job was classified as "definitely" exposed and the second as "probably" exposed to asbestos, then both jobs would be classified as "definite" because the first job contributed the majority (75%) of work time to the combined job category. The only combined jobs that were classified as "not exposed" to asbestos were those in which each component job was considered not to be exposed, as mentioned above.

We examined the influence of asbestos exposure on the lung cancer results in several ways. First, we computed the lung cancer Standardized Mortality Ratios (SMR) relative to mortality rates in U.S. white males during 1942-87 for: 1) the entire group of 2,266 workers included in the re-analysis; 2) the subset of workers who had either "probable" or "definite" asbestos exposure, of any duration, at any times during employment at Manville; and 3) workers who had neither "probable" nor "definite" exposure to asbestos at Manville.

Next, SMRs were computed for joint strata of workers defined by cumulative exposures to crystalline silica and asbestos. The crystalline silica index and the corresponding exposure strata were the same as reported in the original study [Checkoway et al., 1993]. As in the original study, cumulative exposures were lagged by 15 years to allow for a period of disease latency. Cumulative exposures to asbestos were computed using the quantitative exposure index derived by Gibbs and Christensen [1994]; a 15-year exposure lag was included here as well. Four increasing strata of cumulative asbestos exposure (fiber/ml x yr) were defined as: 0, >0-<2.7, 2.7-<6.8, and ≥6.8. Boundaries for the greater than 0 fiber/ml x yr strata were set to permit comparability with findings from a well-known study of U.S. asbestos textile workers [Dement et al., 1994]. Statistical test of trends for SMRs [Breslow and Day, 1987] were also performed for categories of cumulative exposures to crystalline and silica and asbestos.

We also conducted SMR analyses with respect to crystalline silica and duration of asbestos exposure. Additionally, lung cancer SMRs were estimated in reference to crystalline silica after sequentially eliminating workers: 1) with any "definite" asbestos exposure; 2) >1 year "definite" exposure; 3) >1 year "probable" exposure; and 4) any asbestos exposure. In these analyses, workers were eliminated based on potential exposures to asbestos at any times during employment at Manville, i.e., without imposing a lag interval. SMR trend tests were included in these analyses.

Finally, internal exposure-response analyses were performed for crystalline silica and asbestos by means of Poisson regression modeling [Breslow and Day, 1987]. Relative risk gradients were computed for each exposure, with and without statistical control for the other. In the controlled analyses, the exposure of interest was treated as a categorical variable whereas the other exposure, considered as a potential confounder, was left in a continuous form. As before, all exposures were lagged by 15 years. Thus, for example, in the trend analysis for the association with crystalline silica, relative risk

estimates were derived for the four crystalline silica index categories (<50, 50-99, 100-199, and ≥200), and asbestos exposure (fiber/ml x years) was a treated as a continuous variable. Statistical control for age, calendar year, duration of follow-up, and ethnicity (Hispanic vs. non-Hispanic) was maintained throughout the internal trend analyses (see Checkoway et al., 1993 for a description of the Poisson regression modeling approach).

The potential for confounding, by cigarette smoking, of the observed association between crystalline silica and lung cancer was examined by two methods adopted in the original study [Checkoway et al., 1993]. We estimated the prevalence of cigarette smoking, by cumulative levels of crystalline silica, that would be required to render the observed exposure-risk relation null. These calculations were performed in reference to the relative risk gradient for crystalline silica, adjusted for asbestos exposure. The second approach was a computation of the joint distribution of crystalline silica exposure and prevalence of cigarette smoking (ever vs. never). Smoking data available from the Manville medical surveillance program were used for this purpose.

Results

The lung cancer SMR among the entire group of 2266 white male workers was 1.41 (52 observed). According to the exposure classification scheme of Gibbs and Christensen [1994], 1268 workers had either "probable" or "definite" asbestos exposure, and 998 had none. The lung cancer SMRs in these two strata were, resepctively, 1.78 (28 observed) and 1.13 (24 observed) (Table 1). No exposure or work history lagging was performed in calculating the any of the results in Table 1.

The cross-classification of person-years of observation by categories of crystalline silica and asbestos cumulative exposures are given in Table 2. The majority of person-time falls into the joint lowest stratum of crystalline silica and asbestos (<50/0, respectively). This occurred because all workers' exposures began at zero, and increased over time. The 15-year lag also contributes to the clustering of person-years in the top left cell of the table. It is noteworthy that, in the remainder of the table, person-time is widely distributed, which indicates a low correlation between cumulative exposures to the two agents (a high level of correlation would have been evidenced had most of the person-years been concentrated along the diagonal from top left to bottom right, i.e., from the 50-99/>0-<2.7 to ≥200/≥6.8 cells).

The cross-classified SMR results (Table 3) are numerically unstable because of small numbers of observed lung cancers. Nonetheless, these data permit approximate comparisons of the relative contributions of crystalline silica and asbestos to excess lung cancer mortality. Among workers not exposed to asbestos (top row of data) there is a reasonably consistent pattern of increasing mortality with cumulative exposure to crystalline silica. In contrast, the trend for asbestos exposure among workers with the lowest crystalline silica exposures (left column of data) is irregular. None of the SMR trends with respect to crystalline silica or asbestos exposure reached the conventional level of $p<0.05$ of statistical significance. The excess in the joint stratum of highest crystalline silica and asbestos exposure (SMR=8.31) is striking, despite being based on only 3 deaths.

Cross-classified SMRs with respect to crystalline silica and duration (rather than estimated cumulative exposure) to asbestos (Table 4) show a similar pattern to the data in Table 3, although the joint effect of the two exposures (SMR=2.93 in the highest joint stratum) is less prominent than that seen in Table 3. No trend shown in Table 4 was statistically significant.

SMR trends with respect to crystalline silica were computed after elimination of various subsets of asbestos-exposed workers (Table 5). Elimination of workers from these analyses were based on review of potential asbestos exposures throughout entire employment periods, without regard to lag (latency) interval. Thus, for example, the rightmost column of Table 5 excludes workers who had held jobs entailing either "definite" or "probable" asbestos exposures at any times during their employment at Manville. The lung cancer patterns fluctuate somewhat, but generally demonstrate a consistent pattern of elevated risk in the highest crystalline silica exposure categories. It is noteworthy that increased risks at the highest exposure levels remained evident when all asbestos-exposed workers were eliminated from the analysis (rightmost data column), and that this trend was closest to reaching statistical significance.

The internal exposure-response trend, based on Poisson regression modeling, is consistent with the SMR patterns (Table 6). Control for asbestos exposure made barely perceptible differences in the relative risk estimates, which re-confirms that asbestos was not an important confounder. Also consistent with the SMR findings is the large excess among workers with the highest cumulative asbestos exposures (adjusted RR=4.59 for workers with $\geq$6.8 fiber/ml x yrs), detected from internal risk comparisons (Table 7). In order to assess the relative effects of the two exposures, we computed relative risks

associated with 1 year at 10 cumulative exposure units to crystalline silica (the cohort's mean level) and 1 fiber/ml x yr of asbestos (Table 8). The interpretation of these data is that each increment of exposure of either type would produce a 1 percent increase in lung cancer relative risk compared to the lowest exposure category. Mutual control for the other agent did not alter the slope estimates, which was expected in view of the previously demonstrated absence of confounding. The confidence intervals for these slopes were also remarkably similar. Although the relative risk slopes and associated confidence intervals are similar, they cannot be used to compare the relative potencies of crystalline silica and asbestos because the exposure units for these exposures are quite different.

The smoking prevalence distributions required to eliminate the exposure-response gradient for crystalline silica, adjusted for asbestos exposure, under varying estimates of smoking prevalence in the reference category (ranging from 0.3 to 0.7), are given in Table 9. These estimates were generated under the assumption that there is an independent relative risk of 10 associated with smoking. A very strong relation between smoking and exposure would have been necessary for smoking to have been solely responsible for the observed risk gradient. Moreover, it would be virtually impossible for the relative risks in the highest two exposure categories (1.80, 1.79) to be explained by smoking when the baseline prevalence of smoking is set at 0.7, a value that may even be an underestimate for this cohort. Smoking data from the Manville medical surveillance program could only be examined in relation to exposure for workers born during the years 1900-1939; there was no smoking information for workers in various crystalline silica exposure categories for workers born before and after those dates. Based on the available data, there was no evidence of confounding, as smoking prevalence was uniformly distributed across exposure levels (Table 10).

Discussion

The possibility that the observed association between crystalline silica and lung cancer was confounded by asbestos exposures has been evaluated in the Manville segment of the cohort for which the most reliable asbestos exposure information was available. The asbestos exposure assessment was conducted independently of the previous assessment of crystalline silica exposures, and without knowledge of cohort members' mortality outcomes. Thus, a biased classification scheme is unlikely to have been produced.

Our re-analysis demonstrates that asbestos exposure was not an important confounder. In fact, the amount of confounding from asbestos exposure was at most minor. The lack of correlation between cumulative exposures to crystalline silica and asbestos support this conclusion. Also, a reasonably strong risk gradient was observed with crystalline silica among workers who had no apparent asbestos exposure. This gradient is not as strong as the trend reported previously [Checkoway et al., 1993]. One of the more probable explanations for the apparently diminished lung cancer mortality pattern with crystalline silica is that workers hired before 1930, for whom the original lung cancer excess was largest (SMR=2.63), were not included in this re-analysis. It is also highly unlikely that cigarette smoking was a confounder.

Although asbestos exposure does not appear to have confounded the observed relation of lung cancer with crystalline silica, our findings indicate that asbestos exposure may have contributed to lung cancer risk among some members of the cohort. A firm conclusion cannot be reached regarding the extent of the association of lung cancer mortality with asbestos exposure in the Manville plant because the elevated risk was concentrated among the workers with the heaviest asbestos exposures ($\geq$6.8 fibers/ml x yrs), and was based on only 4 deaths. The data also suggest the possibility of an interaction (synergy) between exposures to crystalline silica and asbestos. Evidence for this is almost entirely due to a large relative excess among workers who experienced the highest cumulative exposures to both dusts. Synergy between lung carcinogens (e.g., radon and tobacco smoke) has been reported in other studies. A fuller evaluation of possible independent and interactive effects of crystalline silica and asbestos in this cohort may be possible when the number of lung cancer deaths increases after the extended mortality follow-up through 1993 is completed.

Radiographic information that is being obtained in the ongoing cohort study update, in particular the prevalence of pleural abnormalities by period of employment, should provide further insight into the possible magnitude of asbestos exposure in these DE facilities.

References

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Dement JM, Brown DP, Okun A (1994). Follow-up study of chrysotile asbestos textile workers: cohort mortality and case-control analyses. *Am J Ind Med* 26:431-447.

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Table 1

Lung Cancer Mortality Among 2,266 Manville White Males According to Asbestos Exposure Status*

Group	No. of workers	Observed	SMR†	(95% CI)‡
No asbestos exposure	998	24	1.13	(0.73-1.69)
Any asbestos exposure	1268	28	1.78	(1.18-2.57)
Total	2266	52	1.41	(1.05-1.85)

*Asbestos exposure refers to ever employed in a job, at any time (i.e., without exposure lagging), classified as "definite" or "possible" by Gibbs and Christensen (1994).

†Based on rates for U.S. white males, 1942-87

‡95 percent confidence interval

Table 2

Person-Year Distribution by Cumulative Exposure to Crystalline Silica and Asbestos, Each Lagged 15 Years: 2,266 Manville White Males

Asbestos index (fiber-years)		Crystalline Silica Index† <50 [7.15]*	50-99 [70.0]	100-199 [142]	≥200 [364]
0	[0]*	33,117 (62.1)**	2618 (4.9)	2152 (4.0)	1771 (3.3)
>0-<2.7	[0.95]	6397 (12.0)	1952 (3.7)	1237 (2.3)	744 (1.4)
2.7-<6.8	[4.14]	917 (1.7)	786 (1.5)	474 (0.9)	264 (0.5)
≥6.8	[18.7]	440 (0.8)	142 (0.3)	104 (0.2)	224 (0.4)

†From Checkoway, et al. (1993).

‡Derived from Gibbs and Christensen (1994).

*Mean crystalline silica or asbestos exposure index

**Percent of total (53,339)

Table 3

Lung Cancer Standardized Mortality Ratios (SMR) by Cumulative Exposure to Crystalline Silica and Asbestos, Each Lagged 15 Years: 2,266 Manville White Males

Asbestos index f/ml x yrs	Crystalline Silica Index ≤50 (Obs)	SMR†	50-99 (Obs)	SMR†	100-199 (Obs)	SMR†	≥200 (Obs)	SMR†	Total (Obs)	SMR†	*p*-for trend
0	(15)	1.13 [0.63-1.86]‡	(3)	0.87 [0.18-2.53]	(7)	2.14 [0.86-4.41]	(6)	2.00 [0.73-4.35]	(31)	1.34 [0.91-1.91]	0.12
>0-<2.7	(4)	0.83 [0.23-2.13]	(5)	2.35 [0.76-5.48]	(2)	1.11 [0.13-4.03]	(1)	0.59 [0.01-3.30]	(12)	1.15 [0.59-2.01]	0.92
2.7-<6.8	(3)	4.63 [0.95-13.5]	(1)	1.20 [0.03-6.69]	(1)	1.66 [0.04-9.26]	(0)	0 [0-8.44]	(5)	1.99 [0.65-4.64]	0.12
≥6.8	(0)	0 [0-16.1]	(0)	0 [0-23.8]	(1)	6.03 [0.15-33.6]	(3)	8.31 [1.71-24.3]	(4)	4.40 [1.20-11.3]	0.09
Total	(22)	1.16 [0.73-1.75]	(9)	1.37 [0.62-2.59]	(11)	1.89 [0.94-3.37]	(10)	1.82 [0.87-3.35]	52	(1.41) [1.05-1.85]	0.14
p-for trend	0.46		0.61		0.89		0.23		0.11		

†Based on rates for U.S. white males, 1942-87

‡95 percent confidence interval for SMR

Table 4

Lung Cancer Standardized Mortality Ratios (SMR) by Cumulative Exposure to Crystalline Silica and Duration of Exposure to Any Level of Asbestos*

Duration of asbestos exposure (yrs)	Crystalline Silica Index ≤50 (Obs)	SMR†	50-99 (Obs)	SMR†	100-199 (Obs)	SMR†	≥200 (Obs)	SMR†	Total (Obs)	SMR†	*p*-for trend
0	(15)	1.13 [0.63-1.86]‡	(3)	0.87 [0.18-2.53]	(7)	2.14 [0.86-4.41]	(6)	2.00 [0.73-4.35]	(31)	1.34 [0.91-1.91]	0.12
>0-<5	(7)	1.25 [0.50-2.58]	(5)	1.89 [0.62-4.42]	(2)	1.03 [0.12-3.71]	(0)	0 [0-3.28]	(14)	1.24 [0.68-2.08]	0.39
≥5	(0)	0 [0-36.9]	(1)	2.10 [0.05-11.7]	(2)	3.26 [0.39-11.8]	(4)	2.93 [0.80-7.51]	(7)	2.74 [1.10-5.65]	0.63
Total	(22)	1.16 [0.73-1.75]	(9)	1.37 [0.62-2.59]	(11)	1.89 [0.94-3.37]	(10)	1.82 [0.87-3.35]	52	(1.41) [1.05-1.85]	0.14
p-for trend	0.89		0.27		0.92		0.71		0.27		

*Each lagged 15 years

†Based on rates for U.S. white males, 1942-87

‡95 percent confidence interval for SMR

Table 5

Lung Cancer Standardized Mortality Ratios (SMR) by Cumulative Exposure to Crystalline Silica, Lagged 15 Years, with Varying Exclusions of Asbestos-Exposed Workers

	Exclusion									
	None		Any "definite" asbestos exposure		"Definite" asbestos exposure≥1 yr		"Probable" asbestos exposure≥1yr		Any asbestos exposure§	
Crystalline Silica Index	(Obs)	SMR†	(Obs)	SMR†	(Obs)	SMR†	(Obs)	SMR†	(Obs)	SMR†
<50	(22)	1.16 [0.73-1.76]‡	(14)	0.97 [0.53-1.63]	(21)	1.17 [0.72-1.79]	(14)	0.96 [0.52-1.61]	(9)	0.78 [0.36-1.48]
50-99	(9)	1.37 [0.63-2.60]	(7)	1.43 [0.57-2.94]	(9)	1.42 [0.65-2.69]	(6)	1.31 [0.48-2.85]	(3)	0.88 [0.18-2.57]
100-199	(11)	1.89 [0.94-3.38]	(10)	1.98 [0.95-3.64]	(11)	1.94 [0.97-3.47]	(8)	1.90 [0.82-3.74]	(7)	2.16 [0.87-4.45]
≥200	(10)	1.82 [0.87-3.35]	(8)	1.59 [0.68-3.13]	(8)	1.54 [0.66-3.04]	(5)	1.47 [0.48-3.43]	(5)	1.71 [0.56-4.00]
Total	(52)	1.41 [1.05-1.85]	(39)	1.33 [0.94-1.81]	(49)	1.40 [1.04-1.85]	(33)	1.23 [0.85-1.73]	(24)	1.13 [0.73-1.69]
p-for trend	0.14		0.12		0.24		0.18		0.05	

†Based on rates for U.S. white males, 1942-87

‡95% confidence for SMR

§Excludes workers classified as having had "definite" or "probable" asbestos exposure, of any duration, at any time during employment at Manville

Table 6

Lung Cancer Relative Risks Associated with Cumulative Exposures to Crystalline Silica, with and without Adjustment for Asbestos Exposure

Crystalline		Without adjustment*		With adjustment*	
silica index	No. deaths	RR†	(95% CI)	RR†	(95% CI)
<50	22	1.00	—	1.00	—
50-99	9	1.38	(0.61-3.09)	1.37	(0.61-3.08)
100-199	11	1.81	(0.83-3.94)	1.80	(0.82-3.92)
≥200	10	1.83	(0.79-4.25)	1.79	(0.77-4.18)

*Adjustment for cumulative f/cc x yr, lagged 15 years

†Relative risk adjusted for age, calendar year, duration of follow-up, ethnicity (Hispanic vs. non-Hispanic), by Poisson regression modeling

Table 7

Lung Cancer Relative Risks Associated with Cumulative Exposures to Asbestos, with and without Adjustment for Crystalline Silica Exposure

Asbestos index		Without adjustment		With adjustment*	
f/ml x yrs	No. deaths	RR†	(95% CI)	RR†	(95% CI)
0	31	1.00	—	1.00	—
>0-<2.7	12	0.99	(0.49-1.98)	0.92	(0.45-1.88)
2.7-<6.8	5	1.99	(0.73-5.42)	1.74	(0.62-4.91)
≥6.8	4	5.62	(1.86-17.0)	4.59	(1.40-15.0)

*Adjustment for cumulative exposure to crystalline silica, lagged 15 years

†Relative risk adjusted for age, calendar year, duration of follow-up, ethnicity (Hispanic vs. non-Hispanic), by Poisson regression modeling

Table 8

Exposure-Response Slopes for Crystalline Silica and Asbestos with Lung Cancer Mortality

Exposure	Slope†	(95% CI)‡
Crystalline silica	1.01	(0.99-1.03)
Crystalline silica - adjusted for asbestos	1.01	(0.99-1.03)
Asbestos	1.01	(0.99-1.03)
Asbestos - adjusted for crystalline silica	1.01	(0.98-1.03)

†Relative risk associated with 1 year at 10 crystalline silica units or with 1 f/ml x yr

‡95 percent confidence interval for slope

Table 9

Proportionate Distribution of Smokers Required to Eliminate Observed Exposure-Response Trend for Crystalline Silica and Lung Cancer, Assuming a 15-Year Latency

Crystalline silica index	Observed RR*	Proportion of smokers in reference group		
		0.30	0.50	0.70
<50	1.00	0.30	0.50	0.70
50-99	1.37	0.45	0.73	1.00
100-199	1.80	0.63	0.99	[1.35]†
≥200	1.79	0.62	0.98	[1.34]†

*Relative risk, adjusted for age, calendar year, duration of follow-up, ethnicity (Hispanic vs. non-Hispanic), cumulative asbestos exposure

†[ ] number larger than 1.00 impossible

Table 10

Smoking Status by Estimated Cumulative Exposure to Crystalline Silica Lagged 15 Years: 1575 White Males Born 1900-1939

Crystalline silica index	No. workers with smoking data	No. of smokers	Percent smokers		
			Crude	Adjusted to birth year of cohort†	Adjusted to birth year of workers with smoking data‡
<50	236	198	0.84	0.82	0.83
50-99	126	111	0.88	0.89	0.88
100-199	100	81	0.81	0.83	0.81
≥200	77	65	0.84	0.84	0.83

†Adjusted to birth year distribution of all 1575 white males born 1900-1939

‡Adjusted to birth year distribution of 539 white males born 1900-1939 with available smoking data